

Bioinorganic Chemistry Meets Microbiology: Copper(II) and Zinc(II) Complexes Doing the Cha-Cha with the C-t-CCL-28 Peptide, Dancing till the End of Microbes

Autorzy

Klaudia Szarszoń

Natalia Baran

Paulina Śliwka

Magdalena Wiloch

Tomasz Janek

Joanna Wątył

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The necessity to move away from conventional antibiotic therapy has sparked interest in antimicrobial peptides (AMPs). One fascinating example is human CCL-28 chemokine produced by acinar epithelial cells in the salivary glands. It can also be released into the oral cavity with saliva, playing a crucial role in oral protection. The C-terminal domain of CCL-28 possesses antifungal and antibacterial properties, which are likely linked to membrane disruption and enzyme leakage. Studies suggest that AMPs can become more potent after they have bound Cu(II) or Zn(II). In many cases, these ions are essential for maximizing effectiveness by altering the peptides' physicochemical properties, such as their local charge or structure. The examined peptide binds Cu(II) and Zn(II) ions very effectively, forming equimolar complexes. Metal ion binding affinity, coordination mode, and antimicrobial activity strongly depend on the pH of the environment. Coordination modes have been proposed based on the results of potentiometric titrations, spectroscopic studies (UV–visible, electron paramagnetic resonance and circular dichroism at different path lengths), and mass spectrometry. The antimicrobial properties of the Cu(II) and Zn(II) complexes with the C-terminal fragment of CCL-28 chemokine have been assessed against fungal and bacterial strains, demonstrating exceptional activity against *Candida albicans* at pH 5.4. Moreover, the complex with Zn(II) ions shows the same activity against the *Streptococcus mutans* bacterium as chloramphenicol, a commonly used antibiotic. Cyclic voltammetry proposed a probable antimicrobial mechanism of the studied Cu(II) complex through the formation of reactive oxygen species, which was also confirmed by tests with ascorbic acid in UV–vis and fluorescence spectroscopic studies.

Słowa kluczowe

Antimicrobial activity, Electron paramagnetic resonance spectroscopy, Ions, Monomers, Peptides and proteins

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